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ORIGINAL ARTICLE

Vegetarianism, low meat consumption and the risk of lung, postmenopausal breast and prostate cancer in a population-based cohort study

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BACKGROUND/OBJECTIVES: The few prospective studies that examined lung, female breast and prostate cancer risk in vegetarians have yielded mixed results, whereas none have studied the effects of low meat diets. Moreover, little is known about the explanatory role of (non-) dietary factors associated with these diets.
SUBJECTS/METHODS: The Netherlands Cohort Study—Meat Investigation Cohort (NLCS-MIC)— is an analytical cohort of 11 082 individuals including 1133 self-reported vegetarians (aged 55–69 years at baseline). At baseline (1986), subjects completed a questionnaire on dietary habits and other risk factors for cancer and were classified into vegetarians ($n = 691$), pescetarians ($n = 389$), 1 day per week ($n = 1388$), 2–5 days per week ($n = 2965$) and 6–7 days per week meat consumers ($n = 5649$).
RESULTS: After 20.3 years of follow-up, 279 lung, 312 postmenopausal breast and 399 prostate cancer cases (including 136 advanced) were available for analyses. After adjustment for confounding variables, we found no statistically significant association between meat consumption groups and the risk of lung cancer. As well, no significant associations were observed for postmenopausal breast and overall prostate cancer. After adjustment for confounders, individuals consuming meat 1 day per week were at a 75% increased risk of advanced prostate cancer compared with 6–7 days per week meat consumers (95%CI 1.03–2.97).
CONCLUSIONS: Vegetarians, pescetarians and 1 day per week meat consumers did not have a reduced risk of lung, postmenopausal breast and overall prostate cancer compared with individuals consuming meat on a daily basis after taking confounders into account.

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INTRODUCTION

Although vegetarian diets are primarily defined by the absence of meat and fish, they are also shown to be associated with high intakes of fruits and vegetables and a favorable distribution of non-dietary factors.[1,2] Consequently, vegetarian diets may reduce the risk of different types of cancers through multiple mechanisms, depending on the etiology and preventability of the tumor.[3,4]

We previously reported a nonsignificantly reduced risk of vegetarian and low meat diets on colorectal, and especially rectal, cancer[5] and set out to study its effect on three other major cancers. Although meat consumption has been hypothesized to be implicated in the etiology of lung, female breast and prostate cancer, data are not consistent across studies and meat subtypes.[6–8] However, on the basis of the existing body of literature, vegetarians may be at a lower risk of developing lung cancer (because of lower smoking rates) and to postmenopausal breast cancer (because of lower alcohol consumption, lower body mass index and higher physical activity levels). Although the role of diet in the etiology of prostate cancer remains poorly understood,[4,9] incidence levels of, especially localized, prostate cancers may be related to prostate-specific antigen (PSA) screening utilization, which was shown to differ between vegetarians and non-vegetarians.[10] Nonetheless, the few prospective cohort studies that intentionally included a large proportion of vegetarians reported mixed and inconsistent results regarding lung, female breast and overall prostate cancer risk,[11–15] whereas no study reported on advanced prostate cancer separately. In addition, no study has investigated the association between very low meat consumption and the risk of these cancers.

Within the 'Netherlands Cohort Study-Meat Investigation Cohort' (NLCS-MIC), we investigated the association of vegetarianism and (low) meat consumption with the risk of lung, postmenopausal breast and prostate cancers, including prostate cancer subgroups by disease stage. We investigated the effect of time of adherence to the dietary regimen, the reliability of self-reported vegetarianism and the contribution of individual dietary and lifestyle factors to the observed risk estimates.

PATIENTS AND METHODS

Study population and cancer follow-up

The NLCS 'Meat Investigation Cohort' (NLCS-MIC) is an analytical cohort embedded in the ongoing prospective Netherlands Cohort Study (NLCS). The NLCS study started in September 1986 and includes 120 852 men and women who were 55–69 years of age at baseline. All of the women included in the cohort were presumed to be post-menopausal. At the start of the study, participants were asked to complete a self-administered questionnaire on demographic characteristics, nutrition, lifestyle, chronic disease status and other potential risk factors for cancer.[16] Traditionally, the NLCS uses the case-cohort design. As a consequence, questionnaire

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data were only available for a subcohort that was randomly selected at baseline and all cancer cases. Because the proportion of people in the lower end of the meat consumption spectrum is small the case-cohort approach was not suited to study the health effects of vegetarian and low-meat diets. However, the first page of the questionnaire was processed for all 120 852 cohort members and contained two generic questions about meat consumption: 'Do you have any special eating habits?', and 'How many days on average per week do you eat meat?' This allowed us to create the NLCS-MIC by combining the random subcohort of 10 000 subjects with all self-reported vegetarians and 1 day per week meat consumers from the total NLCS cohort. The 150 item food frequency questionnaire (FFQ) was then used to systematically categorize NLCS-MIC ($n = 11\ 082$) into five meat consumption categories: confirmed vegetarians ($n = 691$) and pescetarians ($n = 389$), 1 day/week ($n = 1388$), 2–5 day/week ($n = 2965$) and 6–7 day/week meat consumers ($n = 5649$). We defined vegetarians as individuals who consume no meat and fish (including vegans, lacto-ovo-, lacto- and ovo-vegetarians) and pescetarians as individuals who do not eat meat, but do eat fish. As a consequence of the procedure followed, NLCS-MIC also includes 1133 self-reported vegetarians of whom 109 reported to consume meat but were not part of the randomly selected subcohort. These latter individuals are only included when examining the effect of self-reported vegetarian status (either confirmed or not) compared with the complementary group of non-(self-reported) vegetarians and not for all other contrasts. Full details of the study design have been described elsewhere.[1]

We used the full-cohort approach for our analyses in NLCS-MIC. NLCS-MIC is being monitored for cancer occurrence by repeated record linkage to the Netherlands Cancer Registry, the Dutch Pathology Registry and the cause of death registry (Statistics Netherlands), together providing a near 100% coverage.[17] Follow-up for vital status was established by record linkage to the automated municipal population registries and the Central Bureau for Genealogy. Less than 1% of the cohort members were lost to follow-up. The NLCS has been approved by the institutional review boards of the TNO Quality of Life Research Institute (Zeist, The Netherlands) and Maastricht University (Maastricht, The Netherlands), and all participants provided informed consent.

Questionnaire

The FFQ estimated the average frequency and amount of foods and beverages consumed over 12 months preceding baseline. The questionnaire also assessed the time since the start of any special eating habits and weekly frequency of meat consumption (for 0–1 day per week meat consumers), in years until baseline (1986). The FFQ also contained 14 items on the consumption of meat with the hot meal (mainly fresh meat, including chicken), 5 items on the consumption of meat products used as sandwich fillings and three items on fish consumption.

Statistical analyses

We estimated the association between the meat consumption group (confirmed vegetarian, pescetarian, 1 day per week, 2–5 days per week and 6–7 days per week meat consumers (reference group)) and the risk of lung, postmenopausal breast and prostate cancer. In addition, the association of cancer incidence with self-reported vegetarian status (self-reported versus complementary group of non-self-reported-vegetarians) and confirmed vegetarian status (confirmed vegetarian versus complementary group of non-vegetarians) was examined. When we observed a statistically significant association, we investigated to what extent this association could be explained by other dietary and lifestyle variables that are associated with a vegetarian or low-meat diet (that is, meat for 1 day per week). For this, we calculated the percentage change in risk estimate, first adjusting for age and sex, then further adjusting for energy and each food group or lifestyle factor in turn. We also examined the association with meat consumption group and confirmed vegetarian status separately for individuals who had adhered to their diet for a long-term period and a short-term period ($\leqslant$10 years, $>$10 years).

We examined the effect of the following food groups and foods in our analyses (in g per day): fresh meat (beef, pork, minced meat, chicken and liver), processed meat, fish, fresh red meat (fresh meat without chicken) and beef, pork, minced meat, chicken and liver as separate types. For the individual meat types, subjects were classified into non-consumers, and tertiles of consumers (highest tertile as reference group), and as continuous variables (per 25 or 50 g increase). For some meat types, categories were used instead of tertiles (liver: a non-user and a user group ($>$0 g per day); chicken: 0 to $<$6.6, $\geqslant$6.6 to $<$22.8 and $\geqslant$ 22.8 g per day; fish 0 to $<$10, $\geqslant$10 to $<$20 and $\geqslant$ 20 g per day).

For all the above-described contrasts, age- and sex-adjusted and multivariable-adjusted hazard rate ratios (HRs) and their corresponding 95% confidence intervals (95% CI) were estimated using Cox proportional hazards models. The proportional hazards assumption was tested using the scaled Schoenfeld residuals. Sensitivity analyses excluding the first 2 years of follow-up were performed. The covariates included in the multivariable analyses were either *a priori* selected risk factors of lung, postmenopausal breast and prostate cancer, or variables that changed the risk estimates for the meat-consumption group, vegetarian status or total fresh meat intake by 10% or more. For a full list of included covariates, see footnotes of Table 1. The independent contribution of the individual meat categories was examined by constructing addition models that summed to total meat.

To enable the comparison, the age (and sex)-adjusted analyses were restricted to subjects included in multivariable-adjusted models. After 20.3 years of follow-up and exclusion of prevalent cancer cases at baseline, 279 lung cancer cases (ICD-O C34), 312 postmenopausal breast cancer cases (C50) and 399 prostate cancer cases (C61) (including 136 advanced (TNM stage III/IV: T3+, N+ or M1 at diagnosis)) remained eligible for analyses. Linear trends were evaluated with the Wald test by entering the categorical exposure variables as a continuous term in the Cox regression model.

All tests were two-tailed and differences were regarded as statistically significant at $P < 0.05$. All analyses were performed using STATA Statistical Software (Intercooled STATA, version12; Stata-Corp LP, College Station, TX, USA).

RESULTS

The distribution of demographic and (non-) dietary characteristics according to the meat consumption group has already been extensively described.[1] Baseline characteristics for cases and non-cases for the cancers under study are described in Table 2. The imbalanced sex distribution between lung cancer cases and non-cases likely resulted in between-group differences in baseline variables. No large differences between postmenopausal breast cancer cases and non-cases were observed. Advanced stage prostate cancer cases were older and consumed smaller amounts of meat compared with non-cases.

After adjustment for age and sex, a statistically significant reduced risk of lung cancer for vegetarians and pescetarians was found when compared with 6–7 days per week meat consumers (HR:0.44, 95% CI:0.21–0.94, and HR:0.28, 95% CI:0.09–0.88, respectively; Table 1). Further adjustment for confounding attenuated these associations such that they were no longer significant (HR:0.85, 95% CI:0.39–1.84, and HR:0.54, 95% CI:0.17–1.70, respectively). A similar pattern was observed when comparing non-meat consumers with meat consumers, and vegetarians (confirmed or self-reported) with their complementary group of non-vegetarians. There was no evidence of an interaction by sex for any of the comparisons made. However, the number of lung cancer cases among the vegetarians and pescetarians was small ($n = 7$ and $n = 3$, respectively). No statistically significant associations for postmenopausal breast cancer were observed in the age and multivariable adjusted models. Although no associations were observed between the risk of all prostate cancers and the meat consumption group, a statistically significant trend across meat consumption groups was observed for advanced prostate cancer risk after adjustment for confounders ($P = 0.05$). Individuals consuming meat $\leqslant$1 per week had a 67% (95% CI:1.10–2.54) higher risk of advanced prostate cancer compared with those consuming meat for 2 or more days per week. In a lag analysis excluding the first 2 years of follow-up, the findings for the meat consumption group and vegetarian status did not change appreciably (data not shown).

To further unravel how confounding by diet and lifestyle factors affected the observations for lung and advanced prostate cancer, we calculated the percent change in HR across the meat

consumption groups, first adjusted for age (and sex), then further adjusted for energy and each food group, or lifestyle factor in turn (Table 3). Although statistical power was limited, smoking status and duration, but not smoking quantity, contributed most to the observed inverse risk of lung cancer of vegetarians, pescetarians and 1 day per week meat eaters when compared with 6–7 days per week meat eaters. Nonetheless, a model including all dietary variables combined was also able to explain most of the observed

Table 1. Age- (and sex) and multivariable-adjusted hazard rate ratios (HR) and 95% CIs for lung, female breast and overall and advanced prostate cancer according to the meat consumption group, vegetarian status and meat-consumption status

Factor	*Category*	*PY*	*Lung cancer*				
			Cases	*HR*[a]	*95% CI*	*HR*[b]	*95% CI*
Meat consumption group	Vegetarian[c]	11 022	7	0.44	0.21–0.94	0.85	0.39–1.84
	Pescetarian	6299	3	0.28	0.09–0.88	0.54	0.17–1.70
	1 day per wk meat	20 989	27	0.83	0.56–1.25	1.05	0.69–1.60
	2–5 days per wk meat	44 082	72	0.91	0.69–1.20	0.97	0.73–1.28
	6–7 days per wk meat	84 205	170	1 (ref)		1 (ref)	
	P-trend			0.04		0.55	
Vegetarianism	Vegetarian[c]	11 022	7	0.47	0.22–1.00	0.86	0.40–1.85
	Non vegetarian	155 575	272	1 (ref)		1 (ref)	
	Self-defined vegetarian[d]	17 799	11	0.40	0.22–0.73	0.76	0.41–1.41
	Non self-defined vegetarian	150 111	270	1 (ref)		1 (ref)	
Meat consumption	Non meat consumers	17 321	10	0.39	0.21–0.75	0.72	0.38–1.38
	Meat consumers	149 276	269	1 (ref)		1 (ref)	
	⩽ 1 day per wk meat	38 311	37	0.64	0.46–0.91	0.95	0.66–1.36
	>1 day per wk meat	128 287	242	1 (ref)		1 (ref)	
			Female breast cancer				
			Cases	*HR*[e]	*95% CI*	*HR*[f]	*95% CI*
Meat consumption group	Vegetarian[c]	7686	18	0.69	0.42–1.12	0.75	0.45–1.24
	Pescetarian	3778	14	1.10	0.63–1.90	1.20	0.78–2.11
	1 day per wk meat	13 520	51	1.11	0.81–1.54	1.18	0.85–1.65
	2–5 days per wk meat	24 602	86	1.03	0.79–1.35	1.06	0.81–1.39
	6–7 days per wk meat	41 041	139	1 (ref)		1 (ref)	
	P-trend			0.44		0.79	
Vegetarianism	Vegetarian[c]	82 941	18	0.67	0.41–1.07	0.70	0.43–1.14
	Non-vegetarian	7686	290	1 (ref)		1 (ref)	
	Self-defined vegetarian[d]	11 258	40	1.04	0.75–1.45	1.11	0.79–1.57
	Non self-defined vegetarian	80 075	272	1 (ref)		1 (ref)	
Meat consumption	Non-meat consumers	11 464	32	0.79	0.55–1.15	0.85	0.58–1.24
	Meat consumers	79 163	276	1 (ref)		1 (ref)	
	⩽ 1 day per wk meat	24 974	83	0.97	0.75–1.24	1.03	0.79–1.35
	>1 day per wk meat	65 642	225	1 (ref)		1 (ref)	
			All prostate cancers				
			Cases	*HR*[e]	*95% CI*	*HR*[g]	*95% CI*
Meat consumption group	Vegetarian[c]	3354	19	1.16	0.72–1.85	1.18	0.72–1.92
	Pescetarian	2434	17	1.40	0.85–2.29	1.35	0.81–2.23
	1 day per wk meat	7011	40	1.12	0.80–1.57	1.17	0.82–1.66
	2–5 days per wk meat	18 861	102	1.05	0.84–1.34	1.11	0.87–1.40
	6–7 days per wk meat	43 583	218	1 (ref)		1 (ref)	
	P-trend			0.20		0.19	
Vegetarianism	Vegetarian[c]	3354	19	1.11	0.70–1.76	1.09	0.68–1.76
	Non-vegetarian	71 888	377	1 (ref)		1 (ref)	
	Self-defined vegetarian[d]	6433	42	1.27	0.92–1.75	1.25	0.80–1.76
	Non-self-defined vegetarian	69 415	357	1 (ref)		1 (ref)	
Meat consumption	Non-meat consumers	5787	36	1.23	0.87–1.73	1.19	0.83–1.70
	Meat consumers	69 454	360	1 (ref)		1 (ref)	
	⩽ 1 day per wk meat	12 799	76	1.16	0.90–1.49	1.16	0.89–1.52
	>1 day per wk meat	62 443	320	1 (ref)		1 (ref)	

Table 1. (Continued)

Factor	*Category*	*PY*	*Advanced (stage III/IV) prostate cancer*				
			Cases	*HR*[e]	*95%CI*	*HR*[g]	*95%CI*
Meat consumption group	Vegetarian[c]	3354	7	1.31	0.60–2.84	1.47	0.65–3.30
	Pescetarian	2434	7	1.77	0.81–3.84	1.77	0.80–3.91
	1 day per wk meat	7011	19	1.61	0.97–2.67	1.75	1.03–2.97
	2–5 day per wk meat	18 861	31	0.97	0.64–1.48	1.04	0.68–1.59
	6–7 day per wk meat	43 583	72	1 (ref)		1 (ref)	
	P-trend			0.08		0.05	
Vegetarianism	Vegetarian[c]	3354	7	1.21	0.57–2.60	1.25	0.57–2.74
	Non-vegetarian	71 888	129	1 (ref)		1 (ref)	
	Self-defined vegetarian[d]	6433	15	1.35	0.79–2.31	1.36	0.77–2.39
	Non-self-defined vegetarian	69 415	121	1 (ref)		1 (ref)	
Meat consumption	Non-meat consumers	5787	14	1.43	0.82–2.48	1.43	0.80–2.55
	Meat consumers	69 454	122	1 (ref)		1 (ref)	
	⩽ 1 day per wk meat	12 799	33	1.58	1.07–2.34	1.67	1.10–2.54
	>1 day per wk meat	62 443	103	1 (ref)		1 (ref)	

Abbreviations: CI, confidence interval; d, day; HR, hazard ratio; ref, reference; PY, person years at risk; wk, week; y, years. All of the women were presumed to be postmenopausal. [a]Adjusted for age (y) and sex. [b]Adjusted for age (y), total energy intake (kcal), cigarette smoking (never, ever and current), frequency of smoking (n/day), duration of smoking (y), alcohol consumption (g per day), BMI (kg/m^2), non-occupational physical activity (< 30,30–60,60–90, > 90 min/d) and level of education (lower vocational, second and medium vocational, and university and higher vocational). [c]Confirmed vegetarians based on the extensive Food Frequency Questionnaire (defined as individuals who consume a diet void of meat). [d]NLCS-MIC includes 1133 self-defined vegetarians of whom 109 reported to consume meat but were not part of the randomly selected subcohort. These individuals are only included in analyses when comparing all self-defined vegetarians (either confirmed or not) with non-self-defined vegetarians and not for all other contrasts. [e]Adjusted for age (y). [f]Adjusted for age (y), total energy intake (kcal), cigarette smoking (never, ever and current), alcohol consumption (g per day), BMI (kg/m^2), non-occupational physical activity (< 30, 30–60, 60–90, > 90 min/d), level of education (lower vocational, second and medium vocational, and university and higher vocational), family history of breast cancer (yes/no), age menarche (y), age menopause (< 50, ⩾ 50, unknown), age first child (y), hormone replacement therapy (yes/no), use of oral contraceptives (yes/no) and number of children. [g]Adjusted for age (y), total energy intake (kcal), cigarette smoking (never, ever and current), alcohol consumption (g per day), BMI (kg/m^2), non-occupational physical activity (< 30, 30–60, 60–90, > 90 min/d), level of education (lower vocational, second and medium vocational, and university and higher vocational) and family history of prostate cancer (yes/no).

risk reduction for vegetarians, although this may largely result from residual confounding by smoking. In contrast, risk estimates for prostate cancer tended to further increase away from the null after adjustment for dietary and lifestyle factors.

We found no consistent indication that vegetarians and low meat consumers adhering to their diet for more than 10 years had a lower lung, breast and prostate cancer risk compared with short-term adherers (⩽10 years; data not shown).

Low consumption of total fresh meat, fresh red meat, beef, pork and minced meat was associated with a significantly reduced lung cancer risk in the age- and sex-adjusted models. However, these attenuated and were no longer statistically significant after adjustment for confounders (Supplementary Table 1A). No association between postmenopausal breast cancer, overall prostate cancer and any of the meat items was observed (Supplementary Table 1B and C). Individuals reporting not to consume chicken and processed meat were at an increased risk of advanced prostate cancer compared with those in the highest category of consumption after adjustment for confounders (HR:1.88 and HR:1.77, respectively).

DISCUSSION

Results from this prospective cohort study showed that, in age- and sex-adjusted models, vegetarians and pescetarians were at a reduced risk of lung cancer compared with individuals consuming meat on a daily basis. This effect disappeared after taking confounders, especially smoking, into account. We did not observe an association between the meat consumption group and the risk of post-menopausal breast and overall prostate cancer.

Although vegetarians and pescetarians were at a >50% lower risk for lung cancer, this was largely the result of their lower prevalence of smoking. After correcting for smoking, the risk estimates attenuated substantially and were no longer significant. Comparable null findings after multivariable adjustment were previously observed.[11–13] Other factors characteristic for a vegetarian and low meat diet such as dietary fiber intake, and the consumption of fruits and vegetables have also previously been reported to reduce lung cancer risk,[18] but our analyses confirm that these observations are likely due to residual confounding by smoking.

Our null findings regarding post-menopausal breast cancer risk are in line with other prospective studies comparing vegetarians with non-vegetarians and a pooled analysis of five cohort studies on breast cancer mortality. In contrast, the UK Women's Cohort Study reported a lower post-menopausal breast cancer risk among non-meat consumers compared with high meat consumers,[14] although this was not observed in their dietary pattern analyses.[15] Vegetarian diets are rich in fiber and soy. Fiber was associated with a reduced risk of breast cancer in a meta-analysis of prospective studies,[19] and soy contains isoflavones, which have previously been associated with a significant reduced risk of postmenopausal breast cancer in Asian populations.[20] However, compared with the average soy intake in four Asian countries (ranging from 38 to 134 g/day[21]), the soy product intake among vegetarians in our population was likely too low to exert an effect (~15 g per day).

We found no statistically significant association between the meat consumption group and the risk of overall prostate cancer. In contrast, vegetarians were at lower risk of overall prostate cancer in the AHS I[11] after adjustment for age, but this may result from differences in PSA screening practices.[10] Although both the vegetarians and the meat consumers in the AHS were generally non-smokers and non-alcohol users, these results were not reproduced by others who also corrected for additional lifestyle factors.[12,13]

Table 2. Baseline characteristics (means or percent) and dietary intakes of exposures of interest of lung, female breast and prostate cancer cases and non-cases in the NLCS-MIC, 1986–2006

Characteristics	*Lung cancer*		*Female breast cancer*		*Prostate cancer*		
	Non cases	*Cases*	*Non cases*	*Cases*	*Non cases*	*All prostate cancer cases*	*Advanced prostate cancer cases*
N	9494	279	4906	312	4465	399	136
Meat consumption group (%)							
Vegetarian	6%	3%[a]	8%	6%	4%	5%	5%
Pescetarian	4%	1%	4%	5%	3%	4%	5%
1 day per wk meat	13%	10%	15%	17%	9%	10%	14%
2–5 days per wk meat	27%	26%	27%	8%	26%	26%	23%
6–7 days per wk meat	51%	61%	45%	45%	59%	55%	53%
Sex (% men)	45%	85%[a]	0%	0%	100%	100%	100%
Age (y)	61.3 ± 4.2	62.3 ± 4.2	61.4 ± 4.2	61.2 ± 4.3	61.2 ± 4.2	62.1 ± 4.1[a]	62.2 ± 4.0[a]
Current smokers (%)	24%	66%[a]	18%	17%	34%	28%	23%[a]
BMI mean	24.7 ± 3.2	24.6 ± 2.8	24.6 ± 3.6	25.1 ± 3.5[a]	24.8 ± 2.7	24.7 ± 2.2	24.9 ± 2.2
Physical activity (non-occupational) (%)							
< 30 min/day	21%	23%	23%	25%	18%	18%	13%
30–60 min/day	30%	32%	31%	32%	30%	25%	28%
60–90 min/day	23%	16%	24%	22%	20%	26%	26%
> 90 min/day	26%	28%	22%	20%	31%	31%	34%
Level of education (%)							
Low	46%	53%[a]	50%	42%[a]	42%	39%[a]	38%
Medium	37%	35%	38%	47%	36%	31%	34%
High	17%	12%	12%	11%	22%	29%	29%
Supplement use (% users)	35%	24%[a]	42%	43%	26%	26%	21%
Energy (kcal)	1880 ± 518	2081 ± 492[a]	1668 ± 412	1692 ± 406	2134 ± 512	2179 ± 546	2195 ± 474
Fiber (g)	28.2 ± 7.6	27.3 ± 7.3[a]	26.6 ± 6.6	26.8 ± 7.3	30.0 ± 8.1	29.6 ± 7.9	29.6 ± 8.0
Alcohol (g)	9.1 ± 13.7	15.1 ± 16.4[a]	5.3 ± 9.3	6.8 ± 12.0[a]	13.9 ± 16.3	14.7 ± 17.4	14.6 ± 15.1
Total fresh meat (g)[b]	80.4 ± 52.4	96.3 ± 55.4	71.4 ± 50.6	72.4 ± 50.8	92.1 ± 52.7	87.2 ± 52.2	81.2 ± 53.6[a]
Fresh red meat (g)[c]	68.9 ± 48.8	86.2 ± 52.9[a]	61.3 ± 46.6	62.2 ± 46.3	81.3 ± 49.6	76.8 ± 48.9	72.3 ± 49.5[a]
Beef (g)	21.3 ± 23.5	26.5 ± 29.1[a]	18.8 ± 22.3	19.4 ± 20.7	24.7 ± 25.1	23.3 ± 24.0	23.3 ± 25.4
Pork (g)	30.1 ± 29.6	37.5 ± 31.7[a]	26.6 ± 28.1	26.2 ± 27.5	35.1 ± 31.0	33.6 ± 29.6	31.7 ± 28.4
Minced meat (g)	14.8 ± 16.1	17.7 ± 20.6[a]	12.8 ± 14.6	13.2 ± 14.6	17.2 ± 17.8	16.1 ± 17.8	14.7 ± 14.5
Liver (g)	1.6 ± 4.0	2.2 ± 4.9	1.3 ± 3.5	1.6 ± 4.1	1.9 ± 4.4	1.7 ± 4.6	0.95 ± 2.32[a]
Chicken (g)	11.4 ± 14.9	11.1 ± 14.1	10.8 ± 14.7	10.7 ± 17.5	11.9 ± 14.7	11.4 ± 13.4	9.4 ± 12.9[a]
Processed meat (g)	10.8 ± 14.0	15.0 ± 18.8[a]	8.2 ± 11.2	7.2 ± 9.1	14.5 ± 16.8	12.5 ± 15.3	11.0 ± 13.3[a]
Fish (g)	13.0 ± 17.9	14.6 ± 22.1	11.8 ± 16.4	11.5 ± 16.2	14.4 ± 19.4	15.1 ± 18.7	14.1 ± 19.4
Vegetables (g)	200 ± 89	190 ± 85	201 ± 88	211 ± 112	197 ± 88	200 ± 88	200 ± 79
Fruits (g)	186 ± 128	138 ± 113[a]	203 ± 129	213 ± 129	162 ± 124	164 ± 118	157 ± 96
Pulses (g)	10.1 ± 16.8	9.9 ± 14.9	8.8 ± 15.1	9.4 ± 14.1	11.4 ± 18.7	11.4 ± 15.9	12.1 ± 15.7
Soya products (g)	3.1 ± 18.0	0.99 ± 6.1[a]	3.2 ± 21.0	3.6 ± 17.7	2.8 ± 13.5	2.7 ± 11.8	4.0 ± 14.8
Milk (g)	313 ± 207	309 ± 219	313 ± 200	307 ± 193	311 ± 215	311 ± 222	317 ± 194
Cheese (g)	26.0 ± 22.6	23.0 ± 21.1[a]	25.5 ± 21.0	26.8 ± 21.3	26.1 ± 24.1	27.4 ± 24.4	26.4 ± 21.7
Eggs (g)	15.5 ± 11.6	16.9 ± 12.6	14.5 ± 10.7	15.2 ± 11.2	16.8 ± 12.5	16.9 ± 13.0	16.0 ± 14.8

Abbreviations: ANOVA, analysis of variance; wk, week; y, years. All of the women were presumed to be postmenopausal. Mean ± s.d., all such values. [a]Statistically significantly different from non-cases (using the χ^2-test for categorical variables and ANOVA for continuous variables) [b]Intake based on raw meat weight [c]Includes beef, pork, minced meat, liver and other meat

We are the first to investigate vegetarianism and low meat consumption in prostate cancer subgroups based on disease stage. TNM stage was used to differentiate advanced prostate cancers (T3+, N+ or M1 at diagnosis); data on tumor grade (Gleason scale) were not available for the full follow-up period in the NLCS. Contrary to our hypothesis, we observed a statistically significant increased risk of advanced prostate cancer for 1 day per week meat consumers compared with those with the highest meat intake (6/7 days per week). Although previous studies have suggested that risk factors for prostate cancer may differ for advanced and non-advanced tumors,[22–24] our observations are not supported by previous studies examining prostate cancer risk in relation to meat consumption, meat carcinogens and other variables that are characteristic for a low meat diet. In addition, our findings for a reduced risk of advanced prostate cancer with increasing intake of chicken and processed meat are not supported by previous research (for example, Sinha *et al*.[25]). As a consequence, our observation may be due to chance and warrants replication in other studies.

The incidence of female breast and prostate cancers increased after the introduction of screening.[26,27] Although we previously reported a lower breast cancer screening mammography rate among vegetarians (23%) compared with the highest meat consumers (29%),[1] correcting these screening practices did not change our risk estimates noticeably. A recent investigation in the AHS II showed that vegetarians are also less likely to follow

Table 3. Difference in Hazard rate ratios (HR) for lung and advanced prostate cancer between vegetarians, pescetarians, 1 day per wk meat and 6–7 days per wk meat consumers after adjustment for individual dietary and lifestyle factors

Factor adjusted for[a]	*Lung cancer*							*Advanced (Stage III/IV) Prostate Cancer*						
	Vegetarian		*Pescetarian*		*1 day per wk meat*		*6–7 day per wk meat*	*Vegetarian*		*Pescetarian*		*1 day per wk meat*		*6–7 day per wk meat*
	HR	*% Change in HR*	*HR*	*% Change in HR*	*HR*	*% Change in HR*	*HR*	*HR*	*% Change in HR*	*HR*	*% Change in HR*	*HR*	*% Change in HR*	*HR*
Age (and sex)	0.44		0.28		0.83		1 (ref)	1.31		1.77		1.61		1 (ref)
Dietary factors														
Energy (kcal)	0.44	0	0.28	0	0.83	0	1 (ref)	1.39	6	1.82	3	1.75	9	1 (ref)
Energy + alcohol (g)	0.48	9	0.29	4	0.87	5	1 (ref)	1.45	11	1.85	5	1.79	11	1 (ref)
Energy + fiber (g)	0.68	55	0.41	46	1.06	28	1 (ref)	1.87	43	2.34	32	2.04	27	1 (ref)
Energy + fruits (g)	0.52	18	0.33	18	0.90	8	1 (ref)	1.52	16	2.03	15	1.82	13	1 (ref)
Energy + vegetables (g)	0.46	5	0.30	7	0.85	2	1 (ref)	1.41	8	1.85	5	1.76	9	1 (ref)
Energy + pulses (g)	0.45	2	0.29	4	0.84	1	1 (ref)	1.43	9	1.87	6	1.78	11	1 (ref)
Energy + soya products (g)	0.55	25	0.36	29	0.92	11	1 (ref)	1.40	7	1.83	3	1.75	9	1 (ref)
Energy + milk (g)	0.44	0	0.28	0	0.84	1	1 (ref)	1.40	7	1.84	4	1.76	9	1 (ref)
Energy + cheese (g)	0.49	11	0.32	14	0.91	10	1 (ref)	1.52	16	2.03	15	1.89	17	1 (ref)
Energy + eggs (g)	0.44	0	0.28	0	0.83	0	1 (ref)	1.37	5	1.83	3	1.73	7	1 (ref)
Energy + Supplement use (0, 1, $\geqslant$ 2)	0.48	9	0.30	7	0.89	7	1 (ref)	1.66	27	2.10	19	1.98	23	1 (ref)
Full model including dietary factors[b]	0.95	116	0.57	104	1.27	53	1 (ref)	2.31	76	2.88	63	2.39	48	1 (ref)
Lifestyle Factors														
Smoking[c]	0.74	68	0.45	61	1.03	24	1 (ref)	1.34	2	1.72	−3	1.58	−2	1 (ref)
Frequency of sigarette smoking	0.47	7	0.29	4	0.85	2	1 (ref)							
Duration of cigarette use	0.73	66	0.47	68	1.10	33	1 (ref)							
All 3 smoking variables	0.89	102	0.55	96	1.11	34	1 (ref)							
Non occupational physical activity[d]	0.45	2	0.29	4	0.85	2	1 (ref)	1.31	0	1.72	−3	1.59	−1	1 (ref)
BMI (kg/m^2)	0.41	−7	0.26	−7	0.81	−2	1 (ref)	1.39	6	1.88	6	1.67	4	1 (ref)
Level of education[e]	0.53	20	0.33	18	0.92	11	1 (ref)	1.23	−6	1.68	−5	1.56	−3	1 (ref)
Full model including dietary and lifestyle factors[b]	1.26	186	0.70	150	1.17	41	1 (ref)	2.44	86	2.90	64	2.43	51	1 (ref)

Abbreviations: d, day; ref, reference. [a]All adjusted for age (and sex). [b]Including all the above listed variables. [c]Smoking categories: never, ever and current smokers. [d]Non-occupational physical activity categories: $<$30, 30–60, 60–90, $>$ 90 min/d. [e]Level of education categories: lower vocational, second and medium vocational, and university and higher vocational.

prostate cancer screening guidelines compared with non-vegetarians,[10] but this is likely population specific. PSA testing was introduced in the Netherlands after 1994; however, it is still not propagated as a screening tool. In 2001, only 14% of men over 45 years of age in the Netherlands had had a PSA measurement in the previous 5 years.[28] In addition, low meat consumption was only associated with advanced prostate cancer risk in the period before PSA testing was introduced. It therefore seems unlikely that differences in PSA testing participation could be responsible for the differences in risk estimates for advanced prostate cancer between the meat-consumption groups.

We performed a multiperspective approach to study meat consumption and cancer risk in our analyses looking both at meat consumption groups and individual meat items. As a result of the multiple comparisons, some findings may be due to chance. For each cancer end point, we performed 14 tests related to meat consumption (five on diet patterns and nine on individual meat categories). According to the Bonferroni correction (α/n), none of the tests were significant at a P-value $\leqslant 0.003$. In addition, we had limited power to detect associations of moderate size between the meat consumption group and the cancer end points under study. An *ad hoc* power analysis showed that the power to detect a hypothetical 25% reduction in lung cancer risk was 0.44 when comparing self-defined vegetarians with non-self-defined vegetarians. The corresponding power for FFQ-confirmed vegetarians was 0.31. Conversely, we would have a power of 80% to detect minimal effect estimates of 0.66 and 0.61 for the self-defined and the FFQ-confirmed vegetarians, respectively. Strengths of our study include the prospective design, the long, nearly complete follow-up, and detailed information on diet and potential risk factors of cancer. Although our analyses have been performed using baseline FFQ data only, the validity of the FFQ has been tested and shown to be representative for dietary habits over a period of at least 5 years.[29]

In conclusion, vegetarians, pescetarians and low-meat consumers did not have a reduced risk of lung, postmenopausal breast and overall prostate cancer compared with individuals consuming meat on a daily basis after taking confounders, especially smoking, into account.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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